individual's immune system; and

administering a bisphosphonic acid, wherein the bisphosphonic acid is selected from the group consisting of AMP, AEP, pamidronic acid, alendronic acid, AIMP, ibandronic acid, risedronic acid, zoledronic acid, cimadronic acid, and tiludronic acid.

REMARKS

Reconsideration of this application is respectfully requested.

The specification and Abstract have been amended as requested by the Examiner.

Original claims 1-5 have been cancelled and new claims 6-14 have been added.

New independent claims 6, 9, 10 and 14 have been drafted to overcome the rejections under 35 U.S.C. §112.

New claim 6 is directed to a medicament for treating a previously diagnosed inappropriate reaction or over-reaction of an individual's immune system, comprising:

an autoantigen or allergen specific to the inappropriate reaction or over-reaction of the individual's immune system;

a bisphosphonic acid, wherein the bisphosphonic acid is selected from the group consisting of AMP, AEP, pamidronic acid, alendronic acid, AIMP, ibandronic acid, risedronic acid, zoledronic acid, cimadronic acid, and tiludronic acid; and

an excipient.

New claim 9 is directed to a medicament for treating a previously diagnosed inappropriate reaction or over-reaction of an individual's immune system, comprising:

an autoantigen, wherein the autoantigen is selected from the group consisting of nervous system tissue extracts, collagen, thyroglobulin, acetylcholine receptor protein, DNA, islet cell extracts, insulin, liver extracts, adrenal cortex extracts, skin extracts, muscle extracts, haemopoetic cell line extracts, heart extracts, eye lens proteins, S-antigens, gastric cell extracts, parietal cell extracts, intrinsic factor, and intestinal extracts, or allergen, wherein the allergen is selected from the group consisting of pollen, dust, mites, foods, animal danders, and insect venom, specific to the inappropriate reaction or over-reaction of the individual's immune system;

a bisphosphonic acid, wherein the bisphosphonic acid is selected from the group consisting of AMP, AEP, pamidronic acid, alendronic acid, AIMP, ibandronic acid, risedronic acid, zoledronic acid, cimadronic acid, and tiludronic acid; and

an excipient.

New claim 10 is directed to a method for treating a previously diagnosed inappropriate reaction or over-reaction of an individual's immune system, comprising:

administering an autoantigen or allergen specific to the inappropriate reaction or over-reaction of the individual's immune system;

administering a first dose of a bisphosphonic acid; and

administering a second dose of a bisphosphonic acid.

New claim 14 is directed to a method for treating a previously diagnosed inappropriate reaction or over-reaction of an individual's immune system, comprising:

administering an autoantigen, wherein the autoantigen is selected from the group consisting of nervous system tissue extracts, collagen, thyroglobulin, acetylcholine receptor protein, DNA, islet cell extracts, insulin, liver extracts, adrenal cortex extracts, skin extracts, muscle extracts, haemopoetic cell line extracts, heart extracts, eye lens proteins, S-antigens, gastric cell extracts, parietal cell extracts, intrinsic factor, and intestinal extracts, or allergen, wherein the allergen is selected from the group consisting of pollen, dust, mites, foods, animal danders, and insect venom, specific to the inappropriate reaction or over-reaction of the individual's immune system; and

administering a bisphosphonic acid, wherein the bisphosphonic acid is selected from the group consisting of AMP, AEP, pamidronic acid, alendronic acid, AIMP, ibandronic acid, risedronic acid, zoledronic acid, cimadronic acid, and tiludronic acid.

In the office action, the examiner rejected the previous claims under 35 U.S.C. §103(a) as being unpatentable over Kawabe, et al in view of Michael et al.

Kawabe is limited to compounds having a diphosphonate structure for use as an drug for bone metabolic disorders, specifically "an antiinflammatory, analgesic, antirheumatic, bone metabolic disease drug, autoimmune disease drug, infectious disease drug, skin disease drug, antiallergic drug, antioxidant or therapeutic drug for ischemic organ disorders due to its action that includes suppression of IL-1, antioxidation and suppression of bone resorption." (page 36, lines 36-39). However, all benefits can be attributed to it's action as an anti-inflammatory, and no alternative treatment methods for the diseases are disclosed.

Michael is limited to a method for orally administering a therapeutic protein. The problem to be solved was preventing destruction of the delicate protein by gastric or intestinal juices (col. 1, lines 52-57). No alternative treatment methods for the diseases mentioned are disclosed.

As the PTO recognizes in MPEP § 2142:

> *... The examiner bears the initial burden of factually supporting any prima facie conclusion of obviousness. If the examiner does not produce a prima facie case, the applicant is under no obligation to submit evidence of nonobviousness....*

> *...the examiner must step backward in time and into the shoes worn by the hypothetical 'person of ordinary skill in the art' when the invention was unknown and just before it was made.....The examiner must put aside knowledge of the applicant's disclosure, refrain from using hindsight, and consider the subject matter claimed 'as a whole'.*

Here, neither Kawabe, et al nor Michael et al. provides any incentive or motivation supporting the desirability of the combination. Therefore, there is simply no basis in the art for combining the references to support a 35 U.S.C. §103 rejection.

In this context, the MPEP § 2143.01 provides:

> *The mere fact that references <u>can</u> be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. In re Mills, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990).*

It is submitted that the examiner's combination arises solely from hindsight based on the invention without any showing of suggestion, incentive or motivation in either reference for the combination as applied to claim 6, 9,10 and 14. Thus, the examiner's burden of factually supporting a *prima facie* case of obviousness with respect to these claims can clearly not be met in this respect. It thus follows that claim 6, 9, 10 and 14 are allowable.

Dependent claims 7, 8, and 11-13 further limit their respective independent claims in a patentable sense and are therefore also in condition for allowance.

In view of the foregoing, an early formal notice of allowance of claims 6-14 is respectfully requested. Should the Examiner have any questions, he is invited to telephone the undersigned at the telephone number listed below.

Respectfully submitted,

Dated: 8/17/01

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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner For Patents, Washington, D.C. 20231

on August 17, 2001

SANDRA KUBIN